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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09 358,937	07 23 1999	ALLAN C. SPRADLING	PM 254812	2149

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Intellectual Property Group  
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McLean, VA 22102

EXAMINER

WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 07 17 2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/358,937

Applicant(s)

SPRADLING ET AL.

Examiner

Joseph Woitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 19 April 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 11-50 is/are pending in the application.
- 4a) Of the above claim(s) 3, 19-22, 32 and 34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-8, 11-18, 23-31, 33 and 35-50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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***Continued Prosecution Application***

The request filed on April 19, 2002, paper number 18, for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/358,937 is acceptable and a CPA has been established. An action on the CPA follows.

**DETAILED ACTION**

This application is an original application filed July 23, 1999 which claims benefit to provisional application 60/094,008, filed July 24, 1998.

As indicated in Applicants' request for continued prosecution, the after final amendment filed February 19, 2002, paper number 16, has been entered. Claims 9 and 10 have been canceled. Claims 1, 2, 7, 12, 13, 16, 17, 25-27, 33, 35 and 36 have been amended. claims 37-43 have been added. In addition, the preliminary amendment filed April 19, 2002, paper number 19, has been received and entered. Claims 1 and 25 have been amended. Claims 44-50 have been added. Claims 1-8, 11-50 are pending. Claims 3, 19-22, 32 and 34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1, 2, 4-8, 11-18, 23-31, 33, 35-50 are currently under examination.

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***Election/Restriction***

Applicants request rejoinder of claims 12, 13 and 17 with the elected invention.

Applicants note that these claims are directed to subject matter which is encompassed by the elected invention because the stimulation occurs "through" a BMP receptor, not "by" a BMP receptor. See Applicants' amendment filed April 19, 2002, bottom of page 4 through page 5.

Upon consideration of Applicants' arguments Examiner agrees that claims directed to stimulation through Dpp is encompassed by the elected invention. In light of Applicants' arguments and upon review of all the pending claims, claims 11-15 and 17 previously withdrawn have been included in the present examination. Accordingly, claims 1, 2, 4-8, 11-18, 23-31, 33, 35-50 are currently under examination.

This application contains claims drawn to an invention nonelected with traverse in Paper No. 11. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

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### ***Claim Objections***

Claim 33 is objected to because of the following informalities: independent claim 33 has been amended, however the only two steps recited are labeled (c) and (d). Since the claim does not depend on another method it does not consist of initial method steps (a) and (b). Relabelling the method steps (a) and (b) would obviate the basis of the objection.

Appropriate correction is required.

### **Claim Rejections - 35 USC § 112**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 40 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 40 is directed to ectopic expression of Dpp with hsp70-GAL4 and UAS-dpp. Upon review of the present specification, it appears that hsp70-GAL4 and UAS-dpp are vectors which express hsp70 and dpp (see page 16, lines 14-15 in Example 1). It is noted that immediately following the recitation of the vectors, the specification cites Brand and Perrimon, 1993, apparently in reference to these vectors. The reference of Brand and Perrimon is not presently made of record, and upon review of the present disclosure, there is no other support for

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the specific elements or characteristics of polynucleotide sequences for hsp70-GAL4 and UAS-dpp taught in the present specification. Since hsp70-GAL4 and UAS-dpp are specifically claimed and essential to practice the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the vectors are not so obtainable or available, the requirements of 35 U.S.C. 112, regarding "how to make", may be satisfied by a deposit of vectors. It is noted that specification indicates that the vectors were taught in Brand and Perrimon, 1993, but there is no indication in the specification as to public availability of these sequences (specification page 16). If the sequences are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific cell lines have been deposited under the Budapest Treaty and that the cell lines will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement.

It the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

- (a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

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- (b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
- (c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request of for the effective life of the patent, whichever is longer; and,
- (d) a test of viability of the biological material at the time of deposit (see 37 CFR 1.807); and,
- (e) the deposit will be replaced if it should ever become inviable.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-8, 16, 18, 23-31, 33, 35 and 36 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

As noted in the advisory action, the claim amendments have obviated the basis of each of the specific rejections previously set forth.

Newly added claims 46, 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

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Claim 50 is unclear and confusing because it appears to simply recite inherent properties of the Dpp expressed in claim 46. It is unclear how claim 50 further limits claim 46.

Additionally, in light of the embodiments set forth in claim 50, claim 46 is unclear because it appears that Dpp can affect a cell by a means other than being secreted and bound by a BMP receptor.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-8, 11-18, 23, 24, 28-31, 33, 35-39 and 41-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Twombly *et al.*

Claims 1, 2, 4-8, 11-18, 23, 24, 28-31, 33, 35-39 and 41-50 are under 35 U.S.C. 102(b) as being anticipated by Forbes *et al.*

Applicants note that the claims have been amended to recite that the practice of the method results in increased abundance of germline stem cells, encompassing the unexpected result taught in the present specification. Applicants argue that the amount or type of expression of Dpp need not be specifically set forth in the claims to distinguish it over the prior art because



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the prior art does not teach an increased abundance of stem cells. See Applicants amendment, middle of pages 6-7. Applicants arguments have been fully considered but not found persuasive.

The office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed methods are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989). Further, case law teaches that reliance upon inherency is not improper even though rejection is based on Section 103 instead of Section 102. *In re Skoner*, 186 USPQ 80 (CCPA).

As noted in the basis of the previous office actions, Twombly *et al.* teach a transgenic *Drosophila* wherein the transgene expressed is Dpp, a TGF- $\beta$  homolog (page 1556; second column) and that it's signal and signal pathway is required by the germline stem cells (page 1556; middle of first column). Further, experiments in which the sax receptor is knocked-out in germline cells clearly indicates the need for dpp signaling in the germline stem cells (page 1561; first and second column in bridging paragraphs) and is generally supported the experiments set forth in Examples 3 and 4 of the instant specification. As in the instant specification, Twombly *et al.* use structural changes in the fly, such as the final production of oocytes, as a measurement of effect of germline cells. Though Twombly *et al.* do not specifically examine the pluripotent or

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totipotent state of the germline stem cells, the evidence provided in Twombly *et al.* clearly indicated that the method of providing dpp to germline cells would inherently result in the increased abundance of the germline stem cells. In summary, the evidence of record present in Twombly *et al.* clearly indicates that the expression of *dpp* would result in affecting the germline cells of the fly. In view of the teachings of the instant specification as evidenced in the working examples, the method of providing dpp in a transgenic fly as taught by Twombly *et al.* clearly anticipates the claimed invention. Finally, Twombly *et al.* teach the expression and disruption of the sax gene as well as the use of FLP and various alternate forms of dpp (page 1556; materials and methods section). Thus, the claimed invention is anticipated, and therefore, the rejection is maintained.

Similarly, as in Twombly *et al.*, Forbes *et al.* teach the ectopic expression of Dpp in *Drosophila* through the expression of a transgene and observe that expression of Dpp results in a multiplicity of germline cells in the ovary (page 3291; first and second column bridging paragraph and figure 7) and that the expression of dpp in the region containing 2-3 germline stem cells results in the fly containing 16 germ line cells, clearly indicating that the expression of dpp has an effect on the germline cells. In the instant case, the ectopic expression of dpp and the increased number of germline cells observed clearly teaches the limitations of the instantly claimed invention are taught by Forbes *et al.* Finally, Forbes *et al.* teach the expression of several other transgenes such as hh, en, and wg (page 3284; material and methods), and the ptc gene is disrupted resulting in the lack of activity of said gene (page 3285; bottom of first

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column). Thus, the claimed invention is anticipated by the teachings of Forbes *et al.*, and therefore, the rejection is maintained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 25-27 stands rejected under 35 U.S.C. 103(a) as being unpatentable over either Forbes *et al.* or Twombly *et al.* and Lin *et al.*

Applicants do not specifically address the basis of the rejection made under 35 USC 103 beyond the arguments directed towards Forbes *et al.* and Twombly *et al.* As note above and in the previous office actions, Applicants' arguments are not persuasive because Forbes *et al.* or Twombly *et al.* each teach a method wherein Dpp is expressed as a transgene in Drosophila resulting either inherently or as observed by Forbes *et al.* in the increase in germline stem cells. Further, each reference teach the additional expression and disruption of genes in the Drosophila genome. Lin *et al.* is provided only to teach that at the time of filing transfer of germline stem cells into a host Drosophila was routine in the art and used to study the affects on germarial cells. Specifically, Lin *et al.* teach the transfer of germline stem cells into a host Drosophila for the

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study of germarial cells (entire reference; summarized in the abstract). At the time of filing, it would have been *prima facie* obvious for one of ordinary skill in the art at the time of the claimed invention to use the methods of germarial cell transfer as taught by Lin *et al.* to implant the stimulated germline stem cells as taught by Forbes *et al.* and Twombly *et al.* to examine the influence of transgene behavior on oogenesis or other parts of development as Lin *et al.* did for various strains/genotypes of donor and host *Drosophila*. There would have been an reasonable expectation of success given the results of Lin *et al.* with the multiple different strains of *Drosophila* to transfer stimulated germline stem cells as taught in Forbes *et al.* and Twombly *et al.* for the further study of germarial development.

Thus, the claimed invention is *prima facie* obvious, and therefore, the rejection is maintained.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Zhao, G.Q *et al.* Genes Dev 10(13):1657-1669. Zhao, G.Q *et al.* teach that BMP 8B is required for the initiation and maintenance of spermatogenesis in the mouse. The teachings of this reference provides further evidence that family members of TGF- $\beta$  superfamily are important in the development and survival of the germ-cell in other organisms besides the fly. The specific relationship of Dpp and BMP8P is not specifically set forth by Zhao, G.Q *et al.*, nor in the instant specification.

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***Conclusion***

No claim is allowed.

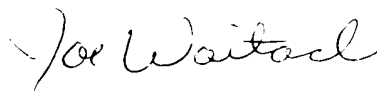
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

  
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